ORIGINAL ARTICLE

Factors Associated with Survival and Mortality of People with Covid-19 Admitted to an Intensive Care Unit

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Highlights:
(1) Mortality from Covid-19 was high.
(2) The chance of survival was greater in women.
(3) Older age, male sex, obesity and hypertension were associated with a higher risk of death.

ABSTRACT

Introduction: Severe acute respiratory syndrome caused by coronavirus disease (Covid-19) spreads rapidly and has unstable behavior. Although most clinical manifestations of Covid-19 are asymptomatic or mild, there are severe forms that require admission to an Intensive Care Unit. *Objective*: to analyze the factors associated with survival and mortality of people with Covid-19 admitted to an intensive care unit. *Method*: This is a retrospective cohort study from March to August 2020, of people with Covid-19 admitted to the intensive care unit of a public hospital that is a reference for treating infectious diseases in the State of Ceará, Brazil. The survival probability was determined using Kaplan Meier, with survival calculations using the R version 3.2 software and comparison between survival curves. A significance level of p=0.05 was considered. *Results*: Of the 92 people with Covid-19, 66.3% were men, obese (23.38%), with cardiovascular disease (19.48%) and HIV (19.48%). A statistically significant difference (p=0.03) was observed with hypertension. The average survival time was 33.93. Mortality from Covid-19 was 69.6%. *Conclusion*: The chance of survival was greater in women. Older age, male sex, obesity and hypertension were associated with a higher risk of death. The results of this study can help managers and healthcare professionals identify high-risk groups that should receive invasive interventions and supportive care.

Keywords: intensive care units; mortality; survival; Covid-19.

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INTRODUCTION

Severe acute respiratory syndrome (SARS) caused by coronavirus disease (Covid-19) has rapid spread and unstable behavior, and was declared by the World Health Organization (WHO)[1] as a Public Health Emergency of International Importance (ESPII) with a pandemic profile.[2]

Although most clinical manifestations of Covid-19 are asymptomatic or mild, there are severe forms of the disease that require admission to the Intensive Care Unit (ICU). Severe Covid-19 is characterized by SARS, sepsis, failure of multiple systems and organs, hyperinflammation, neurological and extrapulmonary manifestations, in addition to thromboembolic disease.[3] Some studies have analyzed the factors that affect morbidity and mortality in patients hospitalized with Covid-19, however few indicate the risk factors that affect the mortality of critically ill patients.[4-5]

A study was conducted in France with 1,045 patients with Covid-19, indicating the need for oxygen (76.7%) of people via nasal cannula or face mask (46.0%), non-invasive mechanical ventilation (2.6%) and invasive mechanical ventilation (28.1%) among patients. The primary outcome occurred on the seventh day of hospitalization in 40.6% of patients, including 32.1% who were admitted to the ICU due to Sars, where 11.0% died, with 2.4% of them in the ICU.[6]

The mortality rate from Covid-19 is estimated at between 1 and 3% of symptomatic patients, with a more significant poor prognosis in adults aged ≥ 60 years, and pre-existing comorbidities such as chronic pneumonitis, obesity, high blood pressure, diabetes, cancer and heart or kidney failure, lymphocytopenia, inflammatory biomarkers, among others.[7] In another study, survival was lower when there was admission to the ICU in people aged ≥ 65 years and with a BMI ≥ 25 kg/m².[6]

Thus, it is clear that decisions to prevent death in the face of critical cases must be based on evidence to guarantee the best possible care. Therefore, it is believed that this study contributes to understanding serious cases and therapeutic guidance. In view of the above, the objective is to analyze the factors associated with survival and mortality of people with Covid-19 admitted to an intensive care unit.

METHOD

This is a retrospective, documentary cohort study of patients diagnosed with Covid-19 admitted to the Intensive Care Unit of a public reference hospital for infectious diseases in Fortaleza, Ceará, Brazil, in 2020. The Strengthening the Reporting guide of Observational Studies in Epidemiology (Strobe) was used to report observational studies.

This study was approved by the Research Ethics Committee of the São José Hospital for Infectious Diseases (HSJDI) under opinion no. 4.301.709 and CAAE 38069820.70000.5044.

Data collection explored the medical records stored in the Medical Archive Service (Same) of the São José Hospital for Infectious Diseases (HSJDI) from March to August 2020 (six months), of patients diagnosed with Covid-19 and who were admitted to the ICU. We included 92 patients, adults, of both sexes, with a diagnosis of Covid-19 confirmed by serological tests for Sars-CoV-2 who were admitted to the ICU during this period.

An adapted and validated instrument was used containing sociodemographic and clinical variables for characterization, survival and mortality: sex, age, medical diagnosis, origin before hospitalization, average time of symptoms before admission to the ICU, comorbidities, clinical outcomes associated with death, discharge and transfer, average survival time, length of stay in the ICU and destination after discharge.

Data were statistically analyzed using the R version 3.2 software (R Foundation for Statistical Computing, Vienna, Austria). Descriptive data analysis and inferential analysis were performed using the

Chi-squared test or Fisher's Exact test (categorical variables) to determine the factors related to mortality and compare the groups of survivors and non-survivors. The magnitude of the association between exposure variables and death was estimated using the odds ratio and relative risk. A normality test was performed for univariate analysis of continuous variables, and depending on the result, the Student's t-test or the non-parametric Mann-Whitney test was used. The significance level was 95% (P<0.05).

A life table based on the Kaplan-Meyer method was constructed to identify the survival rates of patients with Covid-19 admitted to the ICU. Univariate Cox proportional hazards models were fitted to identify possible factors related to survival.

RESULTS

A total of 92 clinical records of Covid-19 cases were analyzed, constituting the total number of patients who were in the ICU during the research period, with an average age of 53.04 ± 17.65 years. The average time of symptoms before admission to the ICU was 2.77 ± 1.17 days.

Table 1 presents the results regarding the demographic distribution and health conditions of the sample during the study period. Most patients were male (66.3%). Regarding serology for COVID-19, 65.2% of the cases analyzed continued even after admission to the ICU and 14 days after the infection diagnosis to test positive for Covid-19 (reactive IgG and IgM). Before progressing to the ICU, 48.9% were previously hospitalized in wards of the same health service.

Regarding the history of comorbidities, 23.38% obesity, 19.48% cardiovascular disease, 19.48% HIV/Aids, 19.48% diabetes, 9.09% chronic hematological disease, 9.09% were diagnosed with hypertension, 2.06% had pneumonia without specific etiology, 1.30% had arrhythmias and 1.30% had a history of liver disease.

In relation to the main clinical outcomes, around 50.0% of patients died, with 69.6% of deaths due to Covid-19.

Table 1 – Distribution in absolute (n) and relative (%) value of data referring to demographic characteristics and health conditions. Fortaleza, CE, Brazil, 2023. (N=92)

	N	%
Sex		
Male	61	66.3
Female	31	33.7
Covid-19 diagnosis		
Negative	32	34.8
Positive	60	65.2
Origin before hospitalization		
Home	19	20.7
HSJ ward	45	48.9
Ward of another hospital	18	19.6
Primary Health Care Unit	10	10.9
Comorbidities		
Other Pneumonias		
Yes	2	2.60
No	75	97.40

Hypertension		
Yes	7	9.09
No	70	90.91
Obesity		
Yes	18	23.38
No	59	76.62
Severe hematological disease		
Yes	7	9.09
No	70	91.91
Cardiovascular disease		
Yes	15	19.48
No	62	80.52
Diabetes		
Yes	10	12.99
No	67	87.01
Immunodeficiency		
Yes	15	19.48
No	62	80.52
Arrhythmias		
Yes	1	1.30
No	76	98.70
Liver disease		
Yes	1	1.30
No	76	98.70
Outcome		
Death	46	50.0
Discharge	6	6.5
Transfer	40	43.5
Death from Covid-19		
Yes	64	69.6
No	28	30.4

Source: Research data.

In the Kaplan-Meier survival analysis of patients with Covid-19 admitted to the ICU (Figure 1), the average survival time was 33.93 ± 4.62 days (Figure 1 A). Regarding sex, the average time was 34.19 ± 5.63 days for males and 35.55 ± 6.27 for females (Figure 1 B).
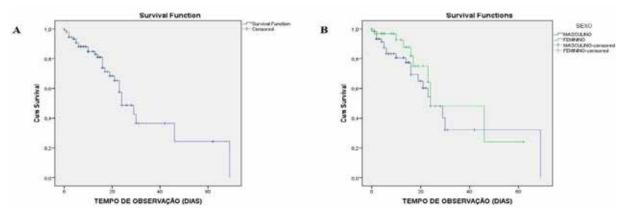
Figure 1 – A- Survival curve due to Covid-19 in the Intensive Care Unit; B – Survival curve due to Covid-19 in the Intensive Care Unit by gender variable. Data analysis from a public hospital in the State of Ceará, Brazil, 2023.

There was no statistically significant difference (p>0.05) in the comparative analysis between the variable of observation time between admission to the ICU and the outcome of death for cases positively diagnosed with Covid-19 and the variables of sex, obesity, chronic hematological disease, cardiovascular disease, diabetes and immunodeficiency (Table 2) using the Student's t-test for independent samples and considering the parametric distribution of the data. However, a significant statistical difference was observed (p=0.03) when analyzing the hypertension variable. It was not possible to analyze the variables of other pneumonias, arrhythmias and liver disease, as they did not satisfy the assumption of counting as valid events in the test.

Table 2 – Comparative analysis of the observation time between ICU admission and death with demographic and clinical variables. Fortaleza, CE, Brazil, 2023. (N=92)

	Mean (standard-deviation)	p-value[*]
Sex		
Male	18.75 (13.22)	0.57
Female	15.15 (15.85)	
Hypertension		
Yes	30.50 (24.47)	0.03
No	12.55 (11.54)	
Obesity		
Yes	22.14 (21.42)	0.20
No	12.82 (12.95)	
Chronic hematological disease		
Yes	12.00 (16.97)	0.75
No	15.86 (16.26)	
Cardiovascular disease		
Yes	20.40 (29.70)	0.45
No	14.26 (11.04)	
Diabetes		
Yes	8.00 (9.19)	0.24
No	17.53 (16.95)	
Immunodeficiency		
Yes	24.25 (14.79)	0.24
No	13.80 (15.97)	

Source: Research data. Student's t-test[*].

Based on these results, it is observed that the average number of hospitalization days in the ICU for individuals diagnosed with Covid-19 is high and a history of systemic arterial hypertension appears to be a significant factor in the association with this outcome.

DISCUSSION

In this study, the average age of people with Covid-19 admitted to the ICU was 53 years old, male and with pre-existing comorbidities. These results corroborate other studies in which high age, presence of associated diseases and being male were more prevalent for infection by Covid-19.[3,9-10]

Covid-19 infection is more likely to affect older men and those with comorbidities; this is observed in other diseases which also have coronavirus as an agent, such as severe acute respiratory syndrome (Sars) and Middle East respiratory syndrome (Mers).[11] It is possible that the higher prevalence in males is related to differences in the levels and types of circulating sex hormones between men and women;[12] this may influence susceptibility to Covid-19, as sex hormones modulate immune responses.[13]

The majority of patients with severe Covid-19 evolved from the ward at the São José Hospital for Infectious Diseases. This data is similar to that reported in another study.[14] The average time of symptoms before admission to the ICU revealed in this study was 2.77, constituting similar data to those found in other studies which evaluated mortality and survival related to Covid-19.[15-16]

A worrying fact was the persistence of positive serology for Covid-19 after 14 days of infection in 65.2% of patients after admission to the ICU, as the virus' activity time in the body is an important marker. This is not only because it is one of the criteria for release from isolation, but since they are individuals with potential for transmission, it is recommended to evaluate the risks of releasing patients with Covid-19 after seven, ten or even 14 days of the positive test, as provided for in the initial protocols to combat Covid-19. Furthermore, this data may reinforce the need for vaccination, maintaining social distancing and the use of masks.[17] Moreover, descriptions of individuals who tested positive for Covid-19, then became negative for the virus, but later became positive again are increasingly common. Both reinfection after new exposure and reactivation of the latent virus may explain these reports.[17]

Other risk factors related to death include hypertension, cardiovascular diseases (CVDs), diabetes, respiratory system diseases and malignancy.[18] This study found that the most common problems in patients with Covid-19 who went to the ICU are obesity, cardiovascular disease, HIV/Aids, diabetes, chronic hematological disease, hypertension, pneumonia without specific etiology, arrhythmias and history of liver disease. Research has shown that patients who required ICU care were older (p<0.001) and were more likely to have underlying comorbidities such as those reported in this study.

Regarding the main clinical outcomes, this study demonstrated that 69.6% of the people who died in the ICU died as a result of Covid-19. The average survival time in the Kaplan-Meier test to analyze the survival of patients with Covid-19 in the ICU was 33.93 days, with differences due to sex, where male individuals have a shorter survival time. Perhaps this fact is associated with circulating levels of angiotensin-converting enzyme 2 (ACE2) receptor, which is related to organic failures, and is higher in male patients with hypertension, diabetes and CVD, who are therefore more prone to die from Covid-19.[19]

It was found that there was no statistically significant difference in the comparative analysis between admission to the ICU and the outcome of death for cases of Covid-19 and the variables of gender, obesity, chronic hematological disease, cardiovascular disease, diabetes and immunodefi-

ciency. However, a significant statistical difference was observed when analyzing the hypertension variable related to the need for intensive care. It is understood that understanding these aspects is important for decision-making, adequate management of patients and their therapeutic regimen, in addition to reducing mortality. Thus, the variables of age, male sex, obesity, cardiovascular disease/ hypertension, need for intensive care and stay in the ICU are factors which are related to a poor prognosis for Covid-19.

This study has some limitations, such as: incomplete information in the medical records; the absence of data such as smoking history and body mass index, potential risk factors for the severity of the disease and mortality; whether there was a need for mechanical ventilation and/or another form of aid in respiratory function; whether or not severe acute respiratory syndrome occurred; and what were the causes that led patients to be admitted to the ICU.

Furthermore, the effect of interventional extracorporeal therapies such as the use of Extracorporeal membrane oxygenation (ECMO), an Elmo helmet or the need for intubation, pronation movements to improve respiratory function, among others which may interfere with survival have not been studied. In addition, laboratory characteristics regarding saturation, a biomarker of nervous changes and tissue hypoperfusion were not observed, as well as not considering the drug therapeutic options used in the ICU to reduce the effects resulting from Covid-19.

In this sense, more studies are needed to analyze all the factors that may be involved and which impact the mortality of critically ill patients related to Covid-19 in the ICU.

CONCLUSION

It was concluded that advanced age, male sex, obesity, hypertension, cardiovascular diseases, diabetes, HIV/Aids and cancer were associated with a worse prognosis for Covid-19 infection. Moreover, 69.6% of the total number of patients who received care in the ICU died as a result of Covid-19, and survival was higher in women.

Based on these results, it is observed that the average number of days spent in the ICU for individuals with Covid-19 is high and a history of systemic arterial hypertension appears to be a significant factor in the association with this outcome.

Due to the pandemic potential of Covid-19, careful surveillance is essential to monitor viral evolution, infectivity, transmissibility, and pathogenicity. The results of this study can help managers and healthcare professionals identify high-risk groups that should receive invasive interventions and supportive care.

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